

WHAT IS CLAIMED IS:

1. A method for synthesizing a plurality of biopolymers at predetermined feature locations on a surface of a substrate wherein one or more of said feature locations comprises degenerate biopolymers, said method comprising, in each round of multiple rounds of subunit additions, providing one or more biopolymer subunit precursors at each of multiple feature locations on said surface to form said plurality of biopolymers on said surface, wherein, for one or more feature locations comprising degenerate biopolymers, said biopolymer subunit precursors comprise a mixture of biopolymer subunit precursors for forming said degenerate biopolymers at said feature location.

2. A method according to Claim 1 wherein said biopolymers are polynucleotides or polypeptides.

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3. A method according to Claim 1 wherein said degenerate biopolymers comprise a contiguous stretch of 1 to 5 degenerate nucleotides.

4. A method for synthesizing a plurality of biopolymers at predetermined feature locations on a surface of a substrate wherein one or more of said feature locations comprise degenerate biopolymers, said method comprising: in each round of multiple rounds of subunit additions, providing one or more biopolymer subunit precursors at each of multiple feature locations on said surface to form said plurality of biopolymers on said surface, wherein, for one or more feature locations comprising degenerate biopolymers, said biopolymer subunit precursors comprise a mixture of biopolymer subunit precursors for forming said degenerate biopolymers at said feature location, each round of subunit additions comprising:

- (a) dispensing from a dispensing system said biopolymer subunit precursors to said discrete sites,
- (b) dispensing activator to said discrete sites, and
- (c) repeating steps (a) – (b).

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5. A method according to Claim 4 wherein said biopolymers are polynucleotides or polypeptides.

6. A method according to Claim 4 wherein said degenerate biopolymers
5 comprise a contiguous stretch of 1 to 5 degenerate nucleotides.

7. A method according to Claim 4 wherein said biopolymers are oligonucleotides.

10 8. A method according to Claim 4 wherein said dispensing system comprises at least one droplet dispensing device.

9. A method according to Claim 4, which is a computer based method wherein steps (a) through (c) are carried out under computer control.

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10. An addressable array prepared by a method according to Claim 1, said array comprising:

(a) a substrate having a surface and
(b) a plurality of features on said surface wherein said features comprise
20 biopolymers and wherein at least one of said features comprises degenerate biopolymers.

11. A method for detecting a target nucleic acid sequence, said method comprising:

25 (a) contacting a medium suspected of containing said target nucleic acid sequence with the array of Claim 10 and
(b) determining a result of said contacting, said result indicating the presence or absence of said target nucleic acid sequence in said medium.

30 12. A method according to Claim 11 wherein said determining of said result comprises examining said array for the presence of a hybrid of said target nucleic acid sequence and a biopolymer specific for said target nucleic acid sequence, the presence

thereof indicating the presence of said target nucleic acid sequence in said medium.

13. An assay result determined by a method according to Claim 11.

5 14. A method comprising forwarding data representing a result obtained by a method of Claim 11.

15 15. A method according to Claim 14 wherein the data is transmitted to a remote location.
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16. A method comprising receiving data representing a result of an interrogation obtained by a method of Claim 11.

17. A method for synthesizing a plurality of oligonucleotides at
15 predetermined sites on a surface of a substrate wherein one or more of said sites comprise a mixture of oligonucleotides that are phylogenetically related, said method comprising:

in each round of multiple rounds of subunit additions, providing one or more nucleotides at each of multiple sites on said surface to form said plurality of
20 oligonucleotides on said surface, wherein, for one or more sites comprising a mixture of phylogenetically related oligonucleotides, said nucleotides comprise a mixture of nucleotides for forming said phylogenetically related oligonucleotides at said site, each round of subunit additions comprising:

- (a) dispensing from a dispensing system said nucleotides to said discrete
25 sites,
- (b) dispensing activator to said discrete sites, and
- (c) repeating steps (a) – (b).

18. A method according to Claim 17 wherein said mixture of nucleotides
30 comprises one or more of dG, T, dC and dA.

19. A method according to Claim 17 wherein said phylogenetically related oligonucleotides comprises 1 to 5 sites of polymorphism.

20. A method according to Claim 17 wherein said oligonucleotides are about 15 to about 60 nucleotides in length.

21. A method according to Claim 17 wherein each different nucleotide of said mixture of nucleotides is dispensed to said site by a separate dispensing nozzle.

22. A method according to Claim 17 wherein each different nucleotide of said mixture of nucleotides is dispensed to said site as a mixture by a single dispensing nozzle.

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23. An addressable array prepared by a method according to Claim 17, said array comprising:

- (a) a substrate having a surface and
- (b) a plurality of sites on said surface wherein said sites comprise oligonucleotides and wherein at least one of said sites comprises a phylogenetically related oligonucleotide.

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24. A method for detecting a target nucleic acid sequence, said method comprising:

- (a) contacting a medium suspected of containing said target nucleic acid sequence with the array of Claim 23 and
- (b) determining a result of said contacting, said result indicating the presence or absence of said target nucleic acid sequence in said medium.

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25. A method according to Claim 24 wherein said determining of said result comprises examining said array for the presence of a hybrid of said target nucleic acid sequence and an oligonucleotide specific for said target nucleic acid sequence, the presence thereof indicating the presence of said target nucleic acid sequence in said medium.

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26. An assay result determined by a method according to Claim 24.

27. An apparatus for synthesizing an array of biopolymers on a surface of a substrate, said apparatus comprising a dispensing device comprising a plurality of nozzle groups, each of said nozzle groups being in fluid communication with a reservoir, at least one of said reservoirs containing a mixture of biopolymer subunit precursors.

5 28. An apparatus according to Claim 27 wherein said mixture of biopolymer subunit precursors comprises a mixture of nucleotide precursors.

29. An apparatus for synthesizing an array of biopolymers on a surface of a substrate, said apparatus comprising:

10 (a) a dispensing device comprising a plurality of nozzle groups, each of said nozzle groups being in fluid communication with a reservoir, each of said reservoirs containing a fluid comprising a single biopolymer subunit precursor, and

 (b) a control unit that activates said dispensing device to dispense one or more drops of fluid comprising said biopolymer subunit precursor at individual feature
15 sites on said surface to deposit a single biopolymer subunit precursor at an individual feature site or to deposit two or more biopolymer subunit precursors at an individual feature site to form a mixture of biopolymer subunit precursors at said individual feature site.

20 30. An apparatus according to Claim 29 wherein said mixture of biopolymer subunit precursors comprises a mixture of nucleotide precursors.

31. A method for normalizing results of binding reactions involving a plurality of samples suspected of containing target molecules and a plurality of arrays,
25 each array comprising features on a surface of a substrate, said method comprising:

 (a) exposing, under binding conditions, a respective array with a respective sample from said plurality of samples wherein each of said arrays comprises a plurality of biopolymers at predetermined feature locations on said surface and wherein one or more of said feature locations on each of said arrays comprise molecules of the same
30 degenerate biopolymers,

 (b) examining said arrays for the results of said binding reactions, and

 (c) employing the results of said binding reactions involving said degenerate

biopolymers to normalize the results of said binding reactions.

32. A method according to Claim 31 wherein said biopolymers are polynucleotides and said binding reactions are hybridization reactions.

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